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GEM-DIFLUOROALLYLLITHIUM: IMPROVED SYNTHESIS
BRINGS IMPROVED APPLICABILITY

by

Dietmar Seyferth, Robert M. Simon,
Dennis J. Sepelak, and Helmut A. Klein

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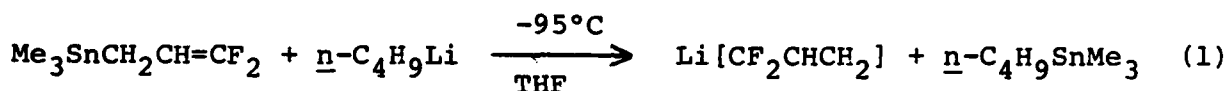
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GEM-DIFLUOROALLYLLITHIUM: IMPROVED SYNTHESIS
BRINGS IMPROVED APPLICABILITY

Sir:

gem-Difluoroallyllithium, I, is of interest as a reagent which allows the introduction of a functional fluorinated substituent into organic and organometallic compounds. We have generated this reagent at low temperature by the transmetalation procedure (eq. 1).¹ The reagent is not stable in solution even at



-95°C and cannot be preformed prior to its reaction with the desired substrate. Its reactions with chlorosilanes were carried out by the in situ procedure: slow addition of n-C₄H₉Li solution to a mixture of Me₃SnCH₂CH=CF₂ and the chlorosilane, so that the reagent is trapped as it is formed. The addition of Li[CF₂CHCH₂] to the C=O of 3-pentanone by the in situ procedure was not successful since the rate of n-butyllithium addition to the ketone is faster than its rate of displacement of the difluoroallyl substituent from tin. Addition of Li[CF₂CHCH₂] to the C=O bond of 3-pentanone to give (C₂H₅)₂-C(OH)CF₂CH=CH₂ (75% yield) was achieved by the method of alternate, incremental additions.¹ However, this procedure is tedious and cumbersome and not well adapted to larger scale application.

In view of these difficulties with Li[CF₂CHCH₂]/carbonyl reactions and also because of the difficult, multi-step preparative route to Me₃SnCH₂CH=CF₂, the Li[CF₂CHCH₂] precursor,¹ we sought an alternative method of generating gem-difluoroallyllithium.

The benzoyl peroxide-induced addition of dibromodifluoromethane to ethylene in an autoclave at 80°C was reported by Tarrant and Lovelace² to give CF₂BrCH₂CH₂Br. The single example of this reaction which was described² involved a runaway exotherm with consequent loss of most of the contents of the autoclave through the rupture disk, but we have used this reaction repeatedly without mishap. In a typical example, the yield of CF₂BrCH₂CH₂Br was 76%, based on unrecovered CF₂Br₂, which had been used in excess. Treatment of CF₂BrCH₂CH₂Br with aqueous KOH at 95-98°C gave a 5:2 mixture (by NMR) of CF₂BrCH=CH₂ and CF₂=CHCH₂Br in 74% yield. Slow distillation of this product mixture gave a distillate with an isomer ratio which had been increased to ca. 20:1. Either isomer mixture serves well as a precursor for gem-difluoroallyllithium (eq. 2)³. In situ



reactions with chlorosilanes gave moderate-to-good yields of 1,1-difluoroallylsilanes. In one such reaction, when 15 mmol of n-butyllithium in hexane was added slowly to a mixture of 19 mmol of 20:1 CF₂BrCH=CH₂/CF₂=CHCH₂Br and 30 mmol of PhMe₂SiCl in 5:1:1 (by volume) THF/Et₂O/pentane at -95°C (under nitrogen, with stirring for 60 min. at -95°C), PhMe₂SiCF₂CH=CH₂¹ was produced in 71% yield. Also prepared in this manner were Et₃SiCF₂CH=CH₂ (51%), n-Pr₃SiCF₂CH=CH₂ (50%) and Me₃SiCF₂CH=CH₂ (89%). In the case of the latter, separation from the n-butyl bromide formed in the Li/Br exchange reaction could not be effected by distillation. However, ethyllithium may be used in place of n-butyllithium to form Li[CF₂CHCH₂] and the ethyl bromide formed in the exchange is much more volatile and does

not interfere in product isolation.

The real utility of this new procedure for $\text{Li}[\text{CF}_2\text{CHCH}_2]$ lies in its applicability to aldehyde and ketone difluoroallylation. In the $\text{Me}_3\text{SnCH}_2\text{CH}=\text{CF}_2/\underline{n}\text{-C}_4\text{H}_9\text{Li}$ route to $\text{Li}[\text{CF}_2\text{CHCH}_2]$ it is a matter of nucleophilic displacement of $[\text{CF}_2\text{CHCH}_2]^-$ from tin by \underline{n} -butyllithium. This polar process is relatively slow at low temperature and cannot compete with the more rapid addition of the lithium reagent to the $\text{C}=\text{O}$ bond. On the other hand, the lithium/halogen exchange reaction, especially when polyhalomethanes are involved, is an electron-transfer process⁴, and, as such, is rapid even at low temperature in ether solvents. Therefore, one might expect that the $\text{CF}_2\text{BrCH}=\text{CH}_2/\underline{n}\text{-C}_4\text{H}_9\text{Li}$ reaction would proceed at a rate comparable to, or even faster than, \underline{n} -butyllithium addition to the carbonyl compound. Such was found to be the case. In situ reactions in which $\text{CF}_2\text{BrCH}=\text{CH}_2/\text{CF}_2=\text{CHCH}_2\text{Br}$ and the aldehyde or ketone in 5:1:1 THF/ Et_2O /pentane solvent at -95°C (under nitrogen, with stirring for 90 min.), with subsequent slow warming to room temperature and hydrolysis, gave alcohols of type $\text{RR}'\text{C}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$ in good yield (by GLC). Thus prepared were $\text{Me}_2\text{C}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$ (41%), $\text{Et}_2\text{C}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$ (70%), cyclo- $\text{C}_6\text{H}_{10}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$ (59%), $\text{PhMeC}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$ (73%), $\underline{n}\text{-C}_4\text{H}_9\text{CH}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$ (87%) and $\text{Me}_3\text{CCH}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$ (95%).⁵

One object of our study of the reactions of gem-difluoroallyllithium with carbonyl compounds was to see if its α/γ regioselectivity in $\text{C}=\text{O}$ additions was the same as or different from that of gem-dichloroallyllithium, a reagent which we had prepared and investigated in an earlier study.⁶ As in the case of $\text{Li}[\text{CCl}_2\text{CHCH}_2]$, the reactions of gem-difluoroallyllithium with aliphatic ketones resulted in C-C bond formation at the halogenated terminus of the re-

agent. However, in contrast to the results obtained in reactions of gem-dichloroallyllithium with aliphatic aldehydes and with acetophenone (mixtures of alcohols, $RR'C(OH)CCl_2CH=CH_2$ and $RR'C(OH)CH_2CH=CCl_2$, in which the former predominated), such reactions of gem-difluoroallyllithium gave only a single product of type $RR'C(OH)CF_2CH=CH_2$. Further work will be aimed at a more detailed comparison of the reactions of $Li[CF_2CHCH_2]$ and $Li[CCl_2CHCH_2]$ using a wider selection of carbonyl substrates.

The $Me_3SnCH_2CH=CF_2/n-C_4H_9Li$ in situ procedure for gem-difluoroallyllithium also failed to give the desired result in the attempted difluoroallylation of dimethyldichlorosilane to $Me_2Si(CF_2CH=CH_2)_2$. Apparently the substitution of the first chlorine by n-butyllithium is faster than its transmetalation with the tin precursor, and $Me_2(n-C_4H_9)SiCF_2CH=CH_2$ was the product which was isolated.¹ In contrast, the rate of the $CF_2BrCH=CH_2/n-C_4H_9Li$ reaction is faster than that of n-butyllithium with dimethyldichlorosilane under the conditions of our experiment, and $Me_2Si(CF_2CH=CH_2)_2$ was obtained in moderate yield.

Using this new and improved route for its generation, we are investigating further aspects of the chemistry of gem-difluoroallyllithium.

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Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Dietmar Seyferth
Robert M. Simon
Dennis J. Sepelak
Helmut A. Klein

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3. In writing eq. 2 we have assumed that it is $\text{CF}_2\text{BrCH}=\text{CH}_2$, not its isomer, which leads to $\text{Li}[\text{CF}_2\text{CHCH}_2]$, in analogy to $\text{RLi/poly-halomethane}$ vs. $\text{RLi/allylic halide}$ reactions. This question, however, will be investigated in future experiments.
4. (a) H. R. Ward, R. G. Lawler and H. Y. Loken, J. Am. Chem. Soc., **90**, 7359 (1968); (b) H. R. Ward, R. G. Lawler and R. A. Cooper, J. Am. Chem. Soc., **91**, 746 (1969); (c) A. R. Lepley and R. L. Landau, J. Am. Chem. Soc., **91**, 748 (1969); (d) A. R. Lepley, Chem. Commun., 64 (1969).
5. All new compounds were characterized by combustion analysis and nmr and ir spectroscopy. The key feature in the proton nmr spectra of these alcohols is the 3-proton multiplet in the vinyl region at about δ 5.2-6.5 ppm and the absence of allylic proton resonances expected between δ 2 and 3 ppm.
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